

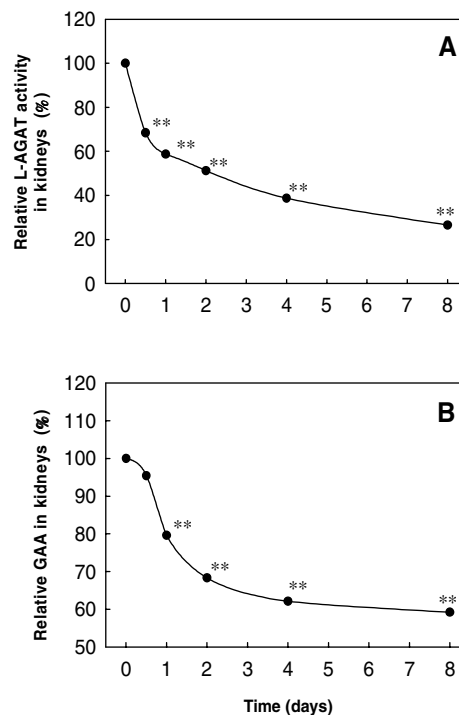
Time-course study of high-dose creatine supplementation for endogenous creatine synthesis

M. Xiang², L. S. Harbige^{2,3}, X. Li¹, B. Li¹ and H. Ai¹

¹Division of Nutrition and Biochemistry, Institute of Sports Medicine, The Third Hospital, Peking University, Beijing, People's Republic of China, ²Centre for Biosciences Research, School of Science, University of Greenwich, Kent ME4 4TB, UK and ³Medway School of Pharmacy, University of Kent and University of Greenwich, Kent ME4 4TB, UK

Creatine (Cre) is a popular nutritional supplement in many population groups, and has potential therapeutic effects in some diseases^(1–4). Cre supplementation may increase the Cre content of muscle⁽⁵⁾, and improve muscle strength⁽⁶⁾. L-Arginine:glycine amidinotransferase (L-AGAT) in the kidney is the rate-limiting enzyme of endogenous Cre synthesis in mammals, and guanidinoacetic acid (GAA) is the precursor in this synthesis. The aim of the present study was to determine the effect of high-dose Cre supplementation on L-AGAT activity and endogenous Cre synthesis. A time-course of repression of L-AGAT activity and GAA concentration by 3.0 g supplemented Cre /kg per d was studied in adult male Sprague-Dawley rats. In the comparison between groups supplemented with 3.0 g Cre/kg body weight per d for 0.5, 1, 2, 4 and 8 d respectively and the control group (without Cre supplementation; *n* 10), the L-AGAT activity in the kidney in the supplemented groups decreased (%) by 31.7, 41.4, 48.9, 61.4 and 73.5 respectively (Fig. 1(A)). Furthermore, the kidney concentration of GAA for the groups receiving 3.0 g Cre/kg per d for 0.5, 1, 2, 4 and 8 d decreased (%) by 4.9, 20.4, 31.7, 37.9 and 40.8 respectively (Fig. 1(B)). The total Cre in gastrocnemius muscle increased gradually with time and was 109.3% above the control levels after 8 d. In the groups receiving 3.0 g Cre/kg per d for 0.5, 1 and 2 d the serum creatinine increased significantly and, then declined gradually until day 8. No significant differences were found in the serum creatine kinase activity among the six groups.

These results indicate that for rats L-AGAT activity and GAA concentration could be repressed rapidly by 3.0 g Cre/kg per d in 8 d, suggesting that high-dose Cre supplementation may quickly result in the depression of endogenous Cre metabolism. These results may be relevant to the immune system and this aspect is currently being investigated in lymphocytes, as little is known about the effect of Cre supplementation on immune cells.



1. Prass K, Royl G, Lindauer U, Freyer D, Megow D, Dirnagl U, Stockler-Ipsiroglu G, Wallimann T & Priller J (2007) *J Cereb Blood Flow Metab* **27**, 452–459.
2. Kley RA, Vorgerd M & Tarnopolsky MA (2007) *Cochrane Database Syst Rev* **1**, CD004760.
3. McMorris T, Harris RC, Swain J, Corbett J, Collard K, Dyson RJ, Dye L, Hodgson C & Draper N (2006) *Psychopharmacology (Berl)* **17**, 1–11.
4. Bender A, Auer DP, Merl T *et al.* (2005) *J Neurol* **252**, 36–41.
5. Rockwell JA, Rankin JW & Toderico B (2001) *Med Sci Sports Exerc* **33**, 61–68.
6. Becque MD, Lochmann JD & Melrose DR (2000) *Med Sci Sports Exerc* **32**, 654–658.